

Amendments to the Claims:

Please enter the following amendments and cancellations without prejudice or disclaimer. This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A method of identifying a target-binding protein that binds to a predetermined target and to a serum albumin, the method comprising:

providing a plurality of at least 10<sup>2</sup> diverse proteins comprising a region encoded by degenerate oligonucleotides; and

identifying one or a subset of members of the plurality which (1) interacts with a predetermined target, other than a serum albumin, and (2) binds to a serum albumin, thereby identifying a target-binding protein that binds to a predetermined target and to a serum albumin.

2. (Currently amended) The method of claim 1, 3, or 65 further comprising evaluating the *in vivo* half life of the identified member or at least some members of the subset.

3. (Currently amended) ~~The method of claim 1,~~ A method of identifying a target-binding protein that binds to a predetermined target and to a serum albumin, the method comprising:

providing a plurality of diverse proteins, wherein the plurality of diverse proteins comprise members of a display library; and

identifying one or a subset of members of the plurality which (1) interacts with a predetermined target, other than a serum albumin, and (2) binds to a serum albumin, thereby identifying a target-binding protein that binds to a predetermined target and to a serum albumin.

4. (Currently amended) The method of claim 1 ~~[[3,]]~~ wherein the identifying comprises screening a display library.

5. (Currently amended) The method of claim 1, 3, or 65 wherein the identifying comprises screening or selecting members of the plurality of diverse proteins that interact with the predetermined target, and then screening or selecting, from those members that interact with the predetermined target, for the one or the subset of members that also bind to serum albumin.

6. (Currently amended) The method of claim 1, 3, or 65 wherein the identifying comprises screening or selecting members of the plurality of diverse proteins that bind to the serum albumin, and then screening or selecting, from those members that bind to the serum albumin, for the one or the subset of members that also interact with the predetermined target.

7. (Currently amended) The method of claim 1, 3, or 65 wherein the serum albumin is human serum albumin.

8. (Currently amended) The method of claim 1, 3, or 65 wherein the predetermined target is an extracellular domain of a naturally occurring protein.

9. (Withdrawn) The method of claim 1 further comprising administering the identified member to a subject.

10. (Withdrawn) The method of claim 1 further comprising formulating the identified member or one or more members of the identified subset as a pharmaceutical composition.

11. (Original) The method of claim 1 wherein each diverse protein comprises a varied peptide of less than 30 amino acids in length.

12. (Original) The method of claim 11 wherein the varied peptide comprises less than 4 constant positions.

13. (Original) The method of claim 11 wherein the varied peptide comprises an intramolecular disulfide bond formed by two invariant cysteine residues.

14. (Currently amended) A target-binding protein isolated by the method of claim 1 and that comprises a polypeptide that has a length less than or equal to 32 amino acids, wherein the peptide that (1) interacts with a predetermined target, other than a serum albumin, and (2) binds to a serum albumin and wherein the peptide does not bind to VEGF-R2.

15. (Withdrawn) A method of identifying a target binding protein, the method comprising:

- (a) providing a plurality of library members, each of which includes a diverse protein;
- (b) identifying a subset of members of the plurality that binds to a predetermined target, other than serum albumin, or to a serum albumin;
- (c) altering the sequence of at least one member of the subset to form an altered subset that includes a plurality of variants of the at least one member; and
- (d) identifying one or a subset of members of the altered subset which binds to (1) the predetermined target if the identifying in (b) is to serum albumin or (2) the serum albumin, if the identifying in (b) is to the predetermined target, thereby identifying a target binding protein.

16. (Withdrawn) The method of claim 15 wherein the altering comprises comparing amino acid sequences of members of the subset, inferring at least one profile for at least some of the members, and preparing the altered library by varying positions not conserved in the at least one profile.

17. (Withdrawn) A method of identifying a target-binding protein that binds to a predetermined target and to a serum albumin, the method comprising:

providing an initial protein that specifically binds to a target compound;

preparing a plurality of variant proteins by altering one or more amino acid positions of the initial protein; and

selecting a target-binding protein that binds to a predetermined target and to a serum albumin from the plurality of variant proteins by evaluating one or more of the variant proteins for binding to the predetermined target and for binding to the serum albumin.

18. (Withdrawn) The method of claim 17 wherein the one or more variant proteins are evaluated by a method that comprises contacting the one or more variant proteins to immobilized serum albumin.

19. (Withdrawn) The method of claim 17 wherein preparing a plurality of variant proteins comprises altering a nucleic acid sequence that encodes the initial protein.

20. (Withdrawn) The method of claim 19 wherein preparing a plurality of variant proteins comprises constructing a display library.

21. (Withdrawn) The method of claim 17 wherein preparing a plurality of variant proteins comprises determining for the initial protein one or more amino acid positions that are non-essential for binding to the predetermined target and varying at least one of the non-essential positions.

22. (Withdrawn) The method of claim 17 wherein preparing a plurality of variant proteins comprises substituting at least one aromatic amino acid into an amino acid position of the initial protein.

23. (Withdrawn) The method of claim 17 wherein providing the initial protein comprises screening a display library.

24. (Withdrawn) An isolated peptide that specifically binds to a target molecule other than serum albumin with a  $K_D$  of less than 1  $\mu$ M and that binds to a serum albumin.

25. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] wherein the peptide has a length of between 6 and 32 amino acids.

26. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] wherein the peptide binds to the serum albumin with a  $K_D$  that is greater than its  $K_D$  for the target molecule.

27. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 26 wherein the peptide binds to the serum albumin with a  $K_D$  that is at least 5 fold greater than its  $K_D$  for the target molecule.

28. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] wherein the peptide has a half-life in vivo of at least 30 minutes in a mouse model system.

29. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] wherein the serum albumin is human serum albumin.

30. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] that comprises an intra-molecular disulfide bond.

31. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] that is attached to a cytotoxic moiety.

32. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] wherein the peptide comprises at least one aromatic an amino acid.

33. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] wherein the peptide comprises an aromatic di- or tri-peptide sequence.

34. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] wherein binding of the peptide to the target molecule and binding of the peptide to the serum albumin are mutually exclusive.

35. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] wherein residues of the peptide that mediate binding to the target molecule and residues that mediate binding to the serum albumin are co-extensive.

36. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] wherein the target molecule comprises an extracellular domain of a naturally occurring protein.

37. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] wherein the target molecule is selected from the group consisting of an integrin, CEA, ~~VEGF-R2~~, and MUC1.

38. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] wherein the peptide and any conjugated moieties has a molecular weight of less than 4500 Daltons.

39. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 38 wherein the peptide and any conjugated moieties has a molecular weight of less than 3500 Daltons.

40. (Withdrawn-currently amended) The ~~peptide~~ protein of claim 14 [[24]] wherein the peptide binds to the target molecule with a  $K_D$  of less than 200 nM.

41.- 45. (Canceled)

46. (Withdrawn) A pharmaceutical composition comprising the peptide of claim 24 and a pharmaceutically acceptable carrier.

47. (Canceled)

48. (Withdrawn) An isolated nucleic acid comprising a sequence that encodes a polypeptide that comprises the peptide of claim 24.

49. (Canceled)

50. (Withdrawn) A recombinant host cell that contains the nucleic acid of claim 48 and that can produce the polypeptide encoded by said nucleic acid.

51.- 57. (Canceled)

58. (Withdrawn) A method of providing an agent, the method comprising: selecting a peptide agent which has been test for ability to bind to a target molecule other than a serum albumin and for ability to bind to serum albumin, thereby providing an agent.

59. (Withdrawn) The method of claim 58 further comprising administering the agent to a subject.

60. (Withdrawn) The method of claim 1 wherein the step of providing a plurality of diverse proteins comprises

providing an initial protein that specifically binds to a target compound, and  
preparing a plurality of variant proteins by altering one or more amino acid positions of the initial protein, thereby providing a plurality of diverse proteins.

61. (Withdrawn) The method of claim 60 wherein preparing a plurality of variant proteins comprises altering a nucleic acid sequence that encodes the initial protein.

62. (Withdrawn) The method of claim 60 that comprises determining for the initial protein one or more amino acid positions that are non-essential for binding to the predetermined target and varying at least one of the non-essential positions.

63. (Withdrawn) The method of claim 60 that comprises substituting at least one aromatic amino acid into an amino acid position of the initial protein.

64. (New) The method of claim 1 or 3, wherein the proteins comprise varied consecutive positions.

65. (New) A method of identifying a target-binding protein that binds to a predetermined target and to a serum albumin, the method comprising:

providing a plurality of diverse proteins, wherein each of the diverse proteins comprises a varied peptide of 30 or less amino acids; and

identifying one or a subset of members of the plurality which (1) interacts with a predetermined target, other than a serum albumin, and (2) binds to a serum albumin, thereby identifying a target-binding protein that binds to a predetermined target and to a serum albumin.



66. (New) The method of claim 65 wherein the varied peptide contains less than three constant positions.

67. (New) The method of claim 65 wherein the varied peptide contains two invariant cysteine residues.

68. (New) The method of claim 65 wherein the varied peptide comprises a varied loop of about 4 to 12 non-cysteine residues.

69. (New) The method of claim 65 wherein the varied peptide is less than 24 amino acids in length.

70. (New) The method of claim 69 wherein the varied peptide is less than 16 amino acids in length.

71. (New) The method of claim 1, 3, or 65 further comprising selecting a protein that binds with higher affinity to the target molecule than the serum molecule.

72. (New) The method of claim 1 or 3, wherein the proteins comprise variants of a scaffold domain.

73. (New) The method of claim 72, wherein the scaffold domain is selected from the group consisting of: a fibronectin Type III repeat, EGF repeat, or a Kunitz domain.